

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
11	BRS	L12	2	3 same 11	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:05			0
12	BRS	L13	26581	(metabolic adj disorder) or (glucose adj tolerance) or (diabetes adj mellitus) or neuropathy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:07			0
13	BRS	L14	75	13 same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:08			0
14	BRS	L15	3	13 same 1 same masked	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:08			0
15	BRS	L16	0	14 same 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:09			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	488	(dipeptidyl adj peptidase adj IV) or (DP adj IV)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 11:34			0
2	BRS	L3	317	1 same inhibit\$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 11:36			0
3	BRS	L4	3	3 same masked	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 11:45			0
4	BRS	L5	47447	(alkyl adj ketone) or (chloroalkyl adj ketone) or cyanide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 11:59			0
5	BRS	L6	1	3 same 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 11:58			0
6	BRS	L7	0	(dipeptide adj alkyl adj ketone) or (dipeptide adj chloroalkyl adj ketone) or (dipeptide adj cyanide)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:01			0
7	BRS	L8	1	(peptide adj alkyl adj ketone) or (peptide adj chloroalkyl adj ketone) or (peptide adj cyanide)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:02			0
8	BRS	L9	4	(peptidyl adj alkyl adj ketone) or (peptidyl adj chloroalkyl adj ketone) or (peptidyl adj cyanide)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:02			0
9	BRS	L10	0	9 same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:03			0
10	BRS	L11	6	(Ile-thia) or (ile-pyr) or (val-thia) or (val-pyr)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/16 12:04			0

FILE 'MEDLINE' ENTERED AT 12:16:08 ON 16 JUL 2003

FILE 'CAPLUS' ENTERED AT 12:16:08 ON 16 JUL 2003  
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FILE 'BIOSIS' ENTERED AT 12:16:08 ON 16 JUL 2003  
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FILE 'EMBASE' ENTERED AT 12:16:08 ON 16 JUL 2003  
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FILE 'SCISEARCH' ENTERED AT 12:16:08 ON 16 JUL 2003  
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FILE 'AGRICOLA' ENTERED AT 12:16:08 ON 16 JUL 2003

=> s (DP IV) or (dipeptidyl peptidase iv)  
L1 6267 (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)

=> s l1 (p) inhibt?  
L2 0 L1 (P) INHIBT?

=> s l1 (p) inhibit?  
L3 1882 L1 (P) INHIBIT?

=> s l3 (p) masked  
L4 2 L3 (P) MASKED

=> duplicate remove l4  
DUPLICATE PREFERENCE IS 'CAPLUS, EMBASE'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L4  
L5 1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)

=> d l5 1 ibib abs

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1  
ACCESSION NUMBER: 1982:522831 CAPLUS  
DOCUMENT NUMBER: 97:122831  
TITLE: Dipeptidyl peptidase IV inhibits the polymerization of  
fibrin monomers  
AUTHOR(S): Mentlein, Rolf; Heymann, Eberhard  
CORPORATE SOURCE: Med. Fak., Univ. Kiel, Kiel, D-2300, Fed. Rep. Ger.  
SOURCE: Archives of Biochemistry and Biophysics (1982),  
217(2), 748-50  
CODEN: ABBIA4; ISSN: 0003-9861  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A highly purified \*\*\*dipeptidyl\*\*\* \*\*\*peptidase\*\*\* \*\*\*IV\*\*\*  
(I) from human placenta cleaved glycylproline from the N-terminal end of  
the fibrin .alpha. chain and \*\*\*inhibited\*\*\* the clotting of fibrin  
monomers. This result underlined the importance of the N-terminus of the  
fibrin .alpha. chain as an aggregation site \*\*\*masked\*\*\* by  
fibrinopeptide A. Apparently, I can hinder blood coagulation in intact  
vessels in vivo, because it is located on the surface of the capillary  
endothelium.

=> d his

(FILE 'HOME' ENTERED AT 12:15:44 ON 16 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
12:16:08 ON 16 JUL 2003

L1 6267 S (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)  
L2 0 S L1 (P) INHIBT?  
L3 1882 S L1 (P) INHIBIT?  
L4 2 S L3 (P) MASKED  
L5 1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)

=> s l3 (p) unstable  
L6 12 L3 (P) UNSTABLE

=> duplicate remove l6

DUPLICATE PREFERENCE IS 'MEDLINE CAPLUS, BIOSIS, EMBASE, SCISEARCH'  
 KEEP DUPLICATES FROM MORE THAN 1 FILE? Y/(N):n  
 PROCESSING COMPLETED FOR L6  
 L7 4 DUPLICATE REMOVE L6 (8 DUPLICATES REMOVED)

=> d 17 1-4 ibib abs

L7 ANSWER 1 OF 4

MEDLINE

DUPLICATE 1

ACCESSION NUMBER:

2001410442

MEDLINE

DOCUMENT NUMBER:

21235368

PubMed ID: 11337057

TITLE:

Transbuccal peptide delivery: stability and in vitro permeation studies on endomorphin-1.

AUTHOR:

Bird A P; Faltinek J R; Shojaei A H

CORPORATE SOURCE:

Department of Pharmaceutical Sciences, School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, TX 79106, USA.

SOURCE:

JOURNAL OF CONTROLLED RELEASE, (2001 May 18) 73 (1) 31-6. Journal code: 8607908. ISSN: 0168-3659.

PUB. COUNTRY:

Netherlands

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

200107

ENTRY DATE:

Entered STN: 20010723

Last Updated on STN: 20010723

Entered Medline: 20010719

AB

The purpose of this study was to investigate the feasibility of buccal delivery of a model peptide, endomorphin-1 (ENI), using stability and in vitro permeation studies. ENI is a recently isolated mu-opiate receptor agonist with high selectivity and specificity for this receptor subtype. Stability studies were conducted in various buffers and the drug was shown to be stable in both acidic and basic buffer systems. In the presence of full thickness porcine buccal epithelium, ENI was \*\*\*unstable\*\*\* with only 23.4+/-15.7% intact drug present after 6 h. The region responsible for this degradation was found to coincide with the major barrier region of the buccal epithelium as delineated through stability experiments in the presence of partial thickness buccal epithelium. Various peptidase \*\*\*inhibitors\*\*\* were used to isolate the enzyme(s) responsible for this degradation. Diprotin-A, a potent \*\*\*inhibitor\*\*\* of \*\*\*dipeptidyl\*\*\* \*\*\*peptidase\*\*\* \*\*\*IV\*\*\*, provided significant \*\*\*inhibition\*\*\* of the degradation of ENI in the presence of buccal epithelium. In vitro permeation studies revealed that the permeability coefficient of ENI across porcine buccal epithelium was 5.67+/-4.74x10(-7) cm/s. The enzymatic degradation of ENI was found not to be rate limiting to the drug's permeation across buccal epithelium, as diprotin-A did not increase the permeation of ENI. Sodium glycocholate as well as sodium taurocholate were also ineffective in enhancing the permeation of ENI across porcine buccal epithelium.

L7 ANSWER 2 OF 4

CAPLUS

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ACCESSION NUMBER:

1999:819402

CAPLUS

DOCUMENT NUMBER:

132:36038

TITLE:

Synthesis of prodrugs of \*\*\*unstable\*\*\* \*\*\*dipeptidyl\*\*\* \*\*\*peptidase\*\*\* \*\*\*IV\*\*\* \*\*\*inhibitors\*\*\* for use in treating diabetes

INVENTOR(S):

Demuth, Hans-Ulrich; Schmidt, Jorn; Hoffmann, Torsten; Glund, Konrad

PATENT ASSIGNEE(S):

Probiodrug Gesellschaft Fur Arzneimittelforschung m.b.H., Germany

SOURCE:

PCT Int. Appl., 41 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967279	A1	19991229	WO 1999-EP4381	19990624
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,			

CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
DE 19828114 A1 20000127 DE 1998-19828114 19980624  
CA 2335978 AA 19990229 CA 1999-2335978 19990624  
AU 9947772 A1 20000110 AU 1999-47772 19990624  
AU 758843 B2 20030403  
BR 9911415 A 20010320 BR 1999-11415 19990624  
EP 1090030 A1 20010411 EP 1999-931163 19990624  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO  
JP 2002518518 T2 20020625 JP 2000-555930 19990624  
NO 2000006483 A 20001219 NO 2000-6483 20001219  
US 2001020006 A1 20010906 US 2000-745883 20001221  
PRIORITY APPLN. INFO.: DE 1998-19828114 A 19980624  
WO 1999-EP4381 W 19990624  
OTHER SOURCE(S): MARPAT 132:36038  
GI

/ Structure 1 in file .gra /

AB The invention relates to compds. of \*\*\*unstable\*\*\* \*\*\*inhibitors\*\*\*  
of \*\*\*dipeptidyl\*\*\* \*\*\*peptidase\*\*\* \*\*\*IV\*\*\* ( \*\*\*DP\*\*\*  
\*\*\*IV\*\*\* ) which comprise general formula A-B-C, whereby A represents an  
amino acid, B represents the chem. bond between A and C or an amino acid,  
and C represents an \*\*\*unstable\*\*\* \*\*\*inhibitor\*\*\* of \*\*\*DP\*\*\*  
\*\*\*IV\*\*\*. Such compds. are used for treating altered glucose tolerance,  
glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus,  
diabetic neuropathy, nephropathy, and secondary diseases in mammals caused  
by diabetes mellitus. Thus, (I) was reacted with pyridine to give [(II);  
R = Cbz], which was deprotected to give II (R = H)(III) which is thought  
to undergo an intramol. cyclization (no data) to form the active  
\*\*\*DP\*\*\* \*\*\*IV\*\*\* \*\*\*inhibitor\*\*\*. In 0.1 M HEPES-buffer, pH  
7.6, at 25.degree., III had a half life (before self-cyclization) of 13.3  
min.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 4 MEDLINE DUPLICATE 2  
ACCESSION NUMBER: 1998327123 MEDLINE  
DOCUMENT NUMBER: 98327123 PubMed ID: 9660870  
TITLE: Functional specialization of stable and dynamic  
microtubules in protein traffic in WIF-B cells.  
AUTHOR: Pous C; Chabin K; Drechou A; Barbot L; Phung-Koskas T;  
Settegrana C; Bourguet-Kondracki M L; Maurice M; Cassio D;  
Guyot M; Durand G  
CORPORATE SOURCE: Laboratoire de Biochimie Generale, Equipe d'Accueil 1595,  
Unite de Formation et de Recherche de Pharmacie, Universite  
Paris-Sud, 92296 Chatenay-Malabry, France.  
SOURCE: JOURNAL OF CELL BIOLOGY, (1998 Jul 13) 142 (1) 153-65.  
Journal code: 0375356. ISSN: 0021-9525.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199808  
ENTRY DATE: Entered STN: 19980828  
Last Updated on STN: 19980828  
Entered Medline: 19980820

AB We found that the magnesium salt of ilimaquinone, named 201-F,  
specifically disassembled dynamically \*\*\*unstable\*\*\* microtubules in  
fibroblasts and various epithelial cell lines. Unlike classical tubulin-  
interacting drugs such as nocodazole or colchicine which affect all  
classes of microtubules, 201-F did not depolymerize stable microtubules.  
In WIF-B-polarized hepatic cells, 201-F disrupted the Golgi complex and  
\*\*\*inhibited\*\*\* albumin and alpha1-antitrypsin secretion to the same  
extent as nocodazole. By contrast, 201-F did not impair the transport of  
membrane proteins to the basolateral surface, which was only affected by  
the total disassembly of cellular microtubules. Transcytosis of two  
apical membrane proteins-the alkaline phosphodiesterase B10 and  
\*\*\*dipeptidyl\*\*\* \*\*\*peptidase\*\*\* \*\*\*IV\*\*\* -was affected to the  
same extent by 201-F and nocodazole. Taken together, these results  
indicate that only dynamically \*\*\*unstable\*\*\* microtubules are  
involved in the transport of secretory proteins to the plasma membrane,  
and in the transcytosis of membrane proteins to the apical surface. By  
contrast, stable microtubules, which are not functionally affected by  
201-F treatment, are involved in the transport of membrane proteins to the

basolateral surface. By specifically disassembling highly dynamic microtubules, 201-F is an invaluable tool with which to study the functional specialization of stable and dynamic microtubules in living cells.

L7 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 95220827 EMBASE  
DOCUMENT NUMBER: 1995220827  
TITLE: Amino acid and peptide phosphonate derivatives as specific inhibitors of serine peptidases.  
AUTHOR: Oleksyszyn J.; Powers J.C.  
CORPORATE SOURCE: OsteoArthritis Sciences, Inc., Cambridge, MA 02139, United States  
SOURCE: Methods in Enzymology, (1994) 244/- (423-441).  
ISSN: 0076-6879 CODEN: MENZAU  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Peptidyl derivatives of .alpha.-aminoalkyl phosphonate diphenyl esters have a number of advantages for in vitro and in vivo experiments compared to other commonly used peptide serine peptidase \*\*\*inhibitors\*\*\*. They are easily synthesized, are chemically very stable, and are not alkylating agents such as the commonly used peptide chloromethyl ketone serine peptidase \*\*\*inhibitors\*\*\*. They are more stable than most other organophosphorus \*\*\*inhibitors\*\*\*, including peptidyl derivatives of the .alpha.-aminoalkyl phosphonates, where the phosphonate moiety is chemically activated by the presence of better leaving groups. The .alpha.-aminoalkyl phosphonate diphenyl esters have outstanding stability (t(1/2) usually greater than 4 days at pH 7.5; >24 hr in plasma). Thus, low \*\*\*inhibitor\*\*\* concentrations can effectively control unwanted serine peptidase activity with low \*\*\*inhibitor\*\*\* concentrations over long time periods, which makes them perfect tools for experiments involving cells. Because .alpha.-aminoalkyl phosphonate diphenyl esters are irreversible \*\*\*inhibitors\*\*\*, they offer real advantages in many experimental situations over reversible \*\*\*inhibitors\*\*\* in cases in which it may be necessary to maintain high concentrations of the reversible \*\*\*inhibitor\*\*\* for long time periods. The second-order \*\*\*inhibition\*\*\* rate constants for phosphonate \*\*\*inhibitors\*\*\* are usually not as high as those observed with other types of peptidyl serine peptidase \*\*\*inhibitors\*\*\*. This is compensated for by their high stability and specificity. The irreversible character of the \*\*\*inhibition\*\*\* reaction allows effective \*\*\*inhibition\*\*\* even if the inactivation rate constant is not large. For example, Cbz-Val(P)(OPh)<sub>2</sub> \*\*\*inhibits\*\*\* HLE with a rate constant of 260 M<sup>-1</sup> sec<sup>-1</sup>. Thus at an effective concentration of 10 .mu.M, 50% of the enzyme is inactivated after 4.5 min, and almost no activity is detected after an 11-min incubation time. Frequently there is a need to specifically \*\*\*inhibit\*\*\* serine peptidases in vitro during protein purification procedures or in biological experiments involving cells or tissue culture. Typically, peptide chloromethyl ketone derivatives are used. However, these inactivators are quite nonspecific alkylating agents and experimental results can be misleading. For example, the presence of a chymotrypsin-like enzyme activity on the neutrophil membrane was assumed when \*\*\*inhibition\*\*\* with Tos-Phe-CH<sub>2</sub>Cl resulted in \*\*\*inhibition\*\*\* of the so-called oxidative burst of these cells. However, it has been shown that the targeted protein is not a serine peptidase, and \*\*\*inhibition\*\*\* results from a nonspecific alkylation reaction. As another example of the utility of phosphonates, dipeptide derivatives of .alpha.-aminoalkyl phosphonate diphenyl ester derivatives with a P1 proline residue are effective \*\*\*inhibitors\*\*\* for \*\*\*dipeptidyl\*\*\* - \*\*\*peptidase\*\*\* \*\*\*IV\*\*\*. The corresponding dipeptide boronic acid and chloromethyl ketone derivatives are \*\*\*unstable\*\*\*. In summary, peptidyl derivatives of .alpha.-aminoalkyl phosphonate diphenyl esters are highly specific irreversible \*\*\*inhibitors\*\*\* of serine peptidases and are chemically stable and stable in plasma. They offer a number of advantages over other types of \*\*\*inhibitors\*\*\* currently in use in biological experiments. After reaction with the enzyme, they form very stable enzyme- \*\*\*inhibitor\*\*\* complexes, making them interesting tools for X-ray studies on the active site structure of new serine peptidases.

=> d his

(FILE 'HOME' ENTERED AT 12:15:44 ON 16 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
12:16:08 ON 16 JUL 2003

L1 6267 S (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)  
L2 0 S L1 (P) INHIBIT?  
L3 1882 S L1 (P) INHIBIT?  
L4 2 S L3 (P) MASKED  
L5 1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)  
L6 12 S L3 (P) UNSTABLE  
L7 4 DUPLICATE REMOVE L6 (8 DUPLICATES REMOVED)

=> s (dipeptid? alkyl ketone) or (dipeptid? chloroalkyl ketone) or (dipeptid? cyanide)  
L8 1 (DIPEPTID? ALKYL KETONE) OR (DIPEPTID? CHLOROALKYL KETONE) OR  
(DIPEPTID? CYANIDE)

=> d l8 1 ibib abs

L8 ANSWER 1 OF 1 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
ACCESSION NUMBER: 78:95513 SCISEARCH  
THE GENUINE ARTICLE: EP971  
TITLE: STERIC EFFECTS ON REACTION OF TRIETHYLENETETRAMINE WITH  
NICKEL(II)- \*\*\*DIPEPTIDEAMIDE\*\*\* - \*\*\*CYANIDE\*\*\*  
COMPLEXES  
AUTHOR: PAGENKOPF G K (Reprint); MARCHESE W A  
CORPORATE SOURCE: MONTANA STATE UNIV, DEPT CHEM, BOZEMAN, MT, 59715  
(Reprint)  
COUNTRY OF AUTHOR: USA  
SOURCE: JOURNAL OF COORDINATION CHEMISTRY, (1978) Vol. 7, No. 4,  
pp. 249-252.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: PHYS  
LANGUAGE: ENGLISH  
REFERENCE COUNT: 17

=> d his

(FILE 'HOME' ENTERED AT 12:15:44 ON 16 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
12:16:08 ON 16 JUL 2003

L1 6267 S (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)  
L2 0 S L1 (P) INHIBIT?  
L3 1882 S L1 (P) INHIBIT?  
L4 2 S L3 (P) MASKED  
L5 1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)  
L6 12 S L3 (P) UNSTABLE  
L7 4 DUPLICATE REMOVE L6 (8 DUPLICATES REMOVED)  
L8 1 S (DIPEPTID? ALKYL KETONE) OR (DIPEPTID? CHLOROALKYL KETONE) OR

=> s (peptid? alkyl ketone) or (peptid? chloroalkyl ketone) or (peptid? cyanide)  
L9 13 (PEPTID? ALKYL KETONE) OR (PEPTID? CHLOROALKYL KETONE) OR (PEPTI  
D? CYANIDE)

=> s l9 (p) l3  
L10 0 L9 (P) L3

=> s (metabolic disorder) or (glucose tolerance) or (diabetes mellitus) or neuropathy  
L11 277517 (METABOLIC DISORDER) OR (GLUCOSE TOLERANCE) OR (DIABETES MELLITU  
S) OR NEUROPATHY

=> s l11 (p) l3  
L12 140 L11 (P) L3

=> s l12 (p) (masked or prodrug or unstable)  
L13 6 L12 (P) (MASKED OR PRODRUG OR UNSTABLE)

=> duplicate remove l13  
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS, SCISEARCH'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L13  
L14 6 DUPLICATE REMOVE L13 (0 DUPLICATES REMOVED)

=> d l14 1-6 ibib abs

L14 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2003:334905 CAPLUS

DOCUMENT NUMBER: 138:338500  
TITLE: Novel [REDACTED] peptidyl peptidase IV (DP-IV) [REDACTED] bitors as anti-diabetic agents  
INVENTOR(S): Evans, David Michael; Tartar, Andre  
PATENT ASSIGNEE(S): Ferring B.V., Neth.  
SOURCE: PCT Int. Appl., 44 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035067	A1	20030501	WO 2002-GB4787	20021023
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: GB 2001-25446 A 20011023  
OTHER SOURCE(S): MARPAT 138:338500  
GI

/ Structure 2 in file .gra /

AB The invention relates to a series of \*\*\*prodrugs\*\*\* of \*\*\*inhibitors\*\*\* of \*\*\*DP\*\*\* - \*\*\*IV\*\*\* with improved properties. Claimed compds. I [X = S, CH<sub>2</sub>; R<sub>1</sub> = H, CN; R<sub>2</sub> = (oxa)(thia)alkyl substituted by carbamoyl, (thio)acylamino, sulfonylamino, or amino groups; R<sub>3</sub> = H<sub>2</sub>NCHR<sub>13</sub>CO, H<sub>2</sub>NCHR<sub>14</sub>CONHCHR<sub>15</sub>CO, CR<sub>16</sub>:CR<sub>17</sub>COR<sub>18</sub>, or R<sub>19</sub>O<sub>2</sub>C, where R<sub>13</sub>-R<sub>15</sub> are side chains of the proteinaceous amino acids, R<sub>16</sub> is H, alkyl, or Ph, R<sub>17</sub> is H or alkyl, R<sub>18</sub> is H, alkyl, OH, alkoxy, or Ph; R<sub>19</sub> is (un)substituted alkyl or phenyl] can be used for the treatment of impaired \*\*\*glucose\*\*\* \*\*\*tolerance\*\*\* and type II diabetes. Thus, (2S)-1-[N.alpha.-(1-acetoxyethoxycarbonyl)-N.omega.-(pyrazinyl-2-carbonyl)-L-ornithinyl]pyrrolidine-2-carbonitrile was prepd. via coupling of (2S)-pyrrolidine-2-carbonitrile (prepn. given) with N.alpha.-tert-butoxycarbonyl-N.omega.-(pyrazinyl-2-carbonyl)-L-ornithine, followed by deprotection and acylation with .alpha.-acetoxyethyl p-nitrophenyl carbonate.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 6 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 2000:576230 SCISEARCH

THE GENUINE ARTICLE: 313NK

TITLE: \*\*\*Prodrugs\*\*\* of \*\*\*DP\*\*\* \*\*\*IV\*\*\*  
\*\*\*inhibitors\*\*\* strongly improve incretin-mediated  
\*\*\*glucose\*\*\* \*\*\*tolerance\*\*\*

AUTHOR: Demuth H U (Reprint); Freyse E J; Berg S; Heinke P;  
McIntosh C C H; Pederson R A  
SOURCE: DIABETES, (MAY 2000) Vol. 49, Supp. [1], pp. 944-944.  
Publisher: AMER DIABETES ASSOC, 1660 DUKE ST, ALEXANDRIA, VA 22314.  
ISSN: 0012-1797.

DOCUMENT TYPE: Conference; Journal  
FILE SEGMENT: LIFE; CLIN  
LANGUAGE: English  
REFERENCE COUNT: 0

L14 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:2379 BIOSIS

DOCUMENT NUMBER: PREV200100002379

TITLE: \*\*\*Prodrugs\*\*\* of \*\*\*DP\*\*\* \*\*\*IV\*\*\* -  
\*\*\*inhibitors\*\*\* strongly improve incretin-mediated  
\*\*\*glucose\*\*\* \*\*\*tolerance\*\*\*

AUTHOR(S): Demuth, Hans-Ulrich (1); Hoffmann, Torsten; Freyse, Ernst-Joachim; Berg, Sabine; Heinke, Peter; McIntosh,

CORPORATE SOURCE: Christopher H. S.; Pederson, Raymond A.  
SOURCE: (1) Probioc Research GmbH, Halle/Saale Germany  
Diabetes Research and Clinical Practice, (September, 2000)  
Vol. 50, No. Suppl. 1, pp. S386. print.  
Meeting Info.: 17th International Diabetes Federation  
Congress on Diabetes Research and Clinical Practice  
Mexico-City, Mexico November 05-10, 2000  
ISSN: 0168-8227.  
DOCUMENT TYPE: Conference  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L14 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2000:504563 BIOSIS  
DOCUMENT NUMBER: PREV200000504563  
TITLE: \*\*\*Prodrugs\*\*\* of \*\*\*DP\*\*\* \*\*\*IV\*\*\* -  
\*\*\*inhibitors\*\*\* strongly improve incretin-mediated  
\*\*\*glucose\*\*\* \*\*\*tolerance\*\*\*  
AUTHOR(S): Demuth, Hans-Ulrich (1); Hoffmann, Torsten (1); Glund,  
Konrad (1); Freyse, Ernst-Joachim (1); Berg, Sabine (1);  
Heinke, Peter (1); McIntosh, Christopher H. S. (1);  
Pederson, Raymond A. (1)  
CORPORATE SOURCE: (1) Probioc Research GmbH, Halle Germany  
SOURCE: Regulatory Peptides, (25 October, 2000) Vol. 94, No. 1-3,  
pp. 59. print.  
Meeting Info.: 13th International Symposium on Regulatory  
Peptides Cairns, Queensland, Australia October 22-26, 2000  
ISSN: 0167-0115.  
DOCUMENT TYPE: Conference  
LANGUAGE: English  
SUMMARY LANGUAGE: English

L14 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1999:819402 CAPLUS  
DOCUMENT NUMBER: 132:36038  
TITLE: Synthesis of prodrugs of unstable dipeptidyl peptidase  
IV inhibitors for use in treating diabetes  
INVENTOR(S): Demuth, Hans-Ulrich; Schmidt, Jorn; Hoffmann, Torsten;  
Glund, Konrad  
PATENT ASSIGNEE(S): Probiocdrug Gesellschaft Fur Arzneimittelforschung  
m.b.H., Germany  
SOURCE: PCT Int. Appl., 41 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967279	A1	19991229	WO 1999-EP4381	19990624
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19828114	A1	20000127	DE 1998-19828114	19980624
CA 2335978	AA	19991229	CA 1999-2335978	19990624
AU 9947772	A1	20000110	AU 1999-47772	19990624
AU 758843	B2	20030403		
BR 9911415	A	20010320	BR 1999-11415	19990624
EP 1090030	A1	20010411	EP 1999-931163	19990624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002518518	T2	20020625	JP 2000-555930	19990624
NO 2000006483	A	20001219	NO 2000-6483	20001219
US 2001020006	A1	20010906	US 2000-745883	20001221
PRIORITY APPLN. INFO.:			DE 1998-19828114 A	19980624
			WO 1999-EP4381 W	19990624

OTHER SOURCE(S): MARPAT 132:36038  
GI

AB The invention relates to compds. of \*\*\*unstable\*\*\* \*\*\*inhibitors\*\*\*  
 of \*\*\*dipeptidyl\*\*\* \*\*\*peptidase\*\*\* \*\*\*IV\*\*\* ( \*\*\*DP\*\*\*  
 \*\*\*IV\*\*\* ) which comprise general formula A-B-C, whereby A represents an  
 amino acid, B represents the chem. bond between A and C or an amino acid,  
 and C represents an \*\*\*unstable\*\*\* \*\*\*inhibitor\*\*\* of \*\*\*DP\*\*\*  
 \*\*\*IV\*\*\*. Such compds. are used for treating altered \*\*\*glucose\*\*\*  
 \*\*\*tolerance\*\*\*, glucosuria, hyperlipidemia, metabolic acidosis,  
 diabetes mellitus, diabetic \*\*\*neuropathy\*\*\*, nephropathy, and  
 secondary diseases in mammals caused by diabetes mellitus. Thus, (I) was  
 reacted with pyridine to give [(II); R = Cbz], which was deprotected to  
 give II (R = H)(III) which is thought to undergo an intramol. cyclization  
 (no data) to form the active \*\*\*DP\*\*\* \*\*\*IV\*\*\* \*\*\*inhibitor\*\*\*  
 . In 0.1 M HEPES-buffer, pH 7.6, at 25.degree., III had a half life  
 (before self-cyclization) of 13.3 min.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:819401 CAPLUS

DOCUMENT NUMBER: 132:36037

TITLE: Synthesis and use of prodrugs of dipeptidyl peptidase  
 IV inhibitors

INVENTOR(S): Demuth, Hans-Ulrich; Hoffmann, Torsten; Schlenzig,  
 Dagmar; Manhart, Susanne

PATENT ASSIGNEE(S): Probiobdrug Gesellschaft fur Arzneimittelforschung  
 m.b.H., Germany

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967278	A1	19991229	WO 1999-EP4382	19990624
W:		AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:		GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
DE 19828113	A1	20000105	DE 1998-19828113	19980624
CA 2335992	AA	19991229	CA 1999-2335992	19990624
AU 9949007	A1	20000110	AU 1999-49007	19990624
BR 9911468	A	20010320	BR 1999-11468	19990624
EP 1087991	A1	20010404	EP 1999-932721	19990624
R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO		
NO 2000006484	A	20001219	NO 2000-6484	20001219
US 2002049164	A1	20020425	US 2000-745776	20001222
PRIORITY APPLN. INFO.:			DE 1998-19828113 A	19980624
			WO 1999-EP4382 W	19990624

OTHER SOURCE(S): MARPAT 132:36037

AB The invention relates to \*\*\*prodrug\*\*\* compds. of \*\*\*inhibitors\*\*\*  
 of \*\*\*dipeptidyl\*\*\* \*\*\*peptidase\*\*\* \*\*\*IV\*\*\* ( \*\*\*DP\*\*\*  
 \*\*\*IV\*\*\* ). Said \*\*\*prodrug\*\*\* compds. comprise general formulas  
 (A-B-C), whereby A represents an amino acid, B represents the chem. bond  
 between A and C or an amino acid, and C represents a stabile  
 \*\*\*inhibitor\*\*\* of \*\*\*DP\*\*\* \*\*\*IV\*\*\*. Such \*\*\*prodrug\*\*\*  
 compds. are used for treating altered \*\*\*glucose\*\*\* \*\*\*tolerance\*\*\*  
 , glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus,  
 diabetic \*\*\*neuropathy\*\*\*, nephropathy, and secondary diseases in  
 mammals caused by diabetes mellitus. Thus, Boc-Pro-Ile-OH was coupled  
 with thiazolidine, N-deprotected, reacted with Boc-Gy-OH, and then  
 N-deprotected to give H-Gly-Pro-Ile-R (R = thiazolidine) (I). In in vivo  
 tests using wister rats, H-Ile-R, I, and H-Pro-Ile-R gave blood glucose  
 levels of 74.4, 57.1, and 56.1% (compared to control = 100%) at doses of  
 2.5.mu.M/300 g wt.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 12:15:44 ON 16 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
12:16:08 ON 16 JUL 2003

L1 6267 S (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)  
L2 0 S L1 (P) INHIBT?  
L3 1882 S L1 (P) INHIBIT?  
L4 2 S L3 (P) MASKED  
L5 1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)  
L6 12 S L3 (P) UNSTABLE  
L7 4 DUPLICATE REMOVE L6 (8 DUPLICATES REMOVED)  
L8 1 S (DIPEPTID? ALKYL KETONE) OR (DIPEPTID? CHLOROALKYL KETONE) OR  
L9 13 S (PEPTID? ALKYL KETONE) OR (PEPTID? CHLOROALKYL KETONE) OR (PE  
L10 0 S L9 (P) L3  
L11 277517 S (METABOLIC DISORDER) OR (GLUCOSE TOLERANCE) OR (DIABETES MULL  
L12 140 S L11 (P) L3  
L13 6 S L12 (P) (MASKED OR PRODRUG OR UNSTABLE)  
L14 6 DUPLICATE REMOVE L13 (0 DUPLICATES REMOVED)

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

107.34

107.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-3.26

-3.26

STN INTERNATIONAL LOGOFF AT 12:30:07 ON 16 JUL 2003